Study of the state variation and neural control parameters of the heart*

Jiguang Ge , Senior Member, IEEE, Zheng Xu and Hang Chen**

Department of Biological Science and Technology

Zhejiang University, Hangzhou 310027 China

Abstract-Heart state information and neural control expound by parameters is useful to early diagnose heart diseases. The purpose of this article was to investigate the efficiency of parameters that express heart state variation and neural control. We have studied three kinds of parameters: global, local and dynamic with different methods to extract heart concealed physiological and pathological information with animal models. Pathological notch on QRS complex of electrocardiogram (ECG) is defined as local parameter which is one of high-frequency components (HFCs) and poincare dispersed-dot plots (PDDP) is defined as nonlinear global one. Pathological notching information on the QRS complex is related with myocardial injuries. We have been working on man-made myocardial infarction models to simulate cardiac abnormalities. And we found that both myocardial injury methods could produce good idiosyncratic relationship between injury area model and man-made pathological condition. A large number of repetitive experiments of animal model indicated that the thresholds of pathological notching have about 84 uV amplitude and 3.8 ms width. The PDDP was a good parameter of heart nonlinear state and rate variability and has thresholds about 26000 ms^2 area and 420 ms long axis for human being and 600 ms^2 area and 85 ms long axis for dogs. Both parameters have showed that they sensitive and early response of heart state of pathological variation and also have dynamic characteristics.

Key words: High-Frequency ECG; Notch; Slur; Poincare dispersed-plot; Nonlinear dynamics

I. INTRODUCTION

The cardiac electrical physiology contains abundant physiological and pathological information and appropriates noninvasive detection but it is not enough utilized for diagnosing heart diseases in clinic in the past. Common diagnostic heart diseases with few parameters or with static indices can not exactly present the pathological variation. Up to now, there is not any good way to find early symptoms of heart diseases and to cure them in time currently because the active state of human heart is so complicated and its diversification of effective facts. In the early 1950's Langner reported the first studies of high-frequency ECG (HFECG) (1952) in order to find early symptoms of heart diseases and improve clinical ECG (1). Since 1960's, 1970's and 1980's, some scientists worked on the study of the HFECG in different way (2) - (5). We have also investigated HFECG for more than ten years and got some good result (6)(7). We discovered that high-frequency information (HFI) in ECG have obviously changed and increased while dog heart as a myocardial-diseased model was studied by induced and localized myocardial injury in the dog. There are numbers of changing and increasing of notches and slurs by injecting formalin or ligaturing coronary artery after half or one hour of heart experimental operation. The certain numbers of pattern of HFCs are similar with wide band recording components of the ECG obtained from physical test of normal subjects (human beings) or dogs and other notches are with diseased pattern. It is response of injury very fast and having early diagnostic value.

Vast scientists and physicians have worked on studies of nonlinear dynamics, fractals and chaos in cardiac activity recent years (8). Babloyantz A.et al. have pointed that the common heart activity stems from deterministic dynamics of chaotic nature characterized by correlation dimensions D2 ranging from 3.6 to 5.2 . Zbilut J. P. Et al. have demonstrated an isolated perfused rat heart and found bifurcations and intrinsic chaotic and 1/f dynamic characteristics. And we have also researched nonlinear dynamics of the heart activity. Especially, RR - intervals is important information in diagnose diseases of heart. Lyapunov Spectrum is a main method for processing nonlinear information. We selected 24 data files of ECG from MIT – BIH database in which there are normal

***The project is subsidized by National Nature Science Foundation of China.(39970205, 39270184, 3870613)**

**Address for correspondence: Jiguang Ge, Department of Biology, Zhejiang University, Hangzhou 310027, China.

Report Documentation Page

Report Date	Report Type	Dates Covered (from... to)
25OCT2001	N/A	-

Title and Subtitle Study of the state variation and neural control parameters of the heart	**Contract Number**
	Grant Number
	Program Element Number
Author(s)	**Project Number**
	Task Number
	Work Unit Number
Performing Organization Name(s) and Address(es) Department of Biological Science and Technology Zhejiang University, Hangzhou 310027 China	**Performing Organization Report Number**
Sponsoring/Monitoring Agency Name(s) and Address(es) US Army Research, Development & Standardization Group (UK) PSC 802 Box 15 FPO AE 09499-1500	**Sponsor/Monitor's Acronym(s)**
	Sponsor/Monitor's Report Number(s)

Distribution/Availability Statement
Approved for public release, distribution unlimited

Supplementary Notes
Papers from the 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology, October 25-28, 2001, held in Istanbul, Turkey. See also ADM001351 for entire conference on cd-rom.

Abstract

Subject Terms

Report Classification unclassified	**Classification of this page** unclassified
Classification of Abstract unclassified	**Limitation of Abstract** UU

Number of Pages
4

ECG, pacing ECG, ECG with ventricular arrhythmias and with bundle and analyzed with Lyapunov spectrum. The results showed that the Lyapunov spectrum is different between normal and other three abnormal ECG. This implies the different kinetic characterizations of the heart in the four states could be extracted from ECG. Our investigations also showed that poincare sections, correlation dimensions and entropy of normal and some pathological ECG are significant differences (9) .

II. MATERIAL AND METHODS

Twenty five dogs, weighting from 8 to 15 kilograms, were used to do experiments in more than 10 years. Physical examination of each one was only tested by audio-visual before experiment. After that, they were used as research subjects if the heart is not abnormal. Each one was lightly anaesthetized by an injection of abdominal cavity of 2% pentobarbital and injected with approximately 1 ml per kilogram of body weight in order to reject the myoelectrical interference then wide band electrocardiogram of 12 leads was recorded and formed as contrast pattern with examinational ECG. Next, a thoracotomy was performed and the experiment was started if the heart was normal without congenital and organic diseases. Some dogs were anaesthetized by an injection of abdominal cavity of pentothal but most of them were anaesthetized by 2% pentobarbital and injected with approximately 1.3-1.7ml per kilogram of body weight. A model structure computer system designed by ourselves is used for animal experiments and for real-time acquiring, processing and displaying data so as to guide the experimental process toward correct progress.

For understanding the neural control of the heart with the anaesthetic effect on wide band ECG, we have worked on the expression of wide band ECG on body surface with the different anaesthetic condition and have got significant results. 38% formalin was used to produce acute myocardial injury. Several branches of coronary anterior descending branch near apex and part of blunt edge branch were ligatured for creating chronic pathological changes. Forming injurious models at left ventricular side-wall was expected with above methods. All dogs have been produced injurious model under direct sight through the senses after open chest so as to correctly control the location and level of injury. Then wide band ECG was measured in time and the expressing and changing of wide band ECG and its HFCs are surveyed in time. There were fourteen dogs for chronic observation, and nine dogs were re-operated to examine the results and 7 of the 9 dogs were got their hearts out to cut sections of myocardial tissues for microscopic examination after two month raising.

The six of nine dogs are and were measured with different period using different methods, such as once every half hour, one hour or every 4 hours after heart operation and so on. Then they measured once every day after one day or two days even measured once every two or three days after several days from operation till second operation.

The eight rabbits were used to study nonlinear dynamics of heart activity at clear – headed state but the dogs can not be tested at clear – headed condition because they were feeling afraid investigators to measure them. Those rabbits, weighting from 2.5 – 3.0 kg, were used to do experiments of linear dynamics at clear – headed condition. Physical examination of each one was tested the same with dogs. They were received physical examination and made records used as control sample, then divided five stages and first suffered slight anaesthetized by an injection 1.0 ml of abdominal cavity of 3% pentobarbital for each one, then measured wide band ECG after five minutes. After that, every two days after their clear – headed injected anesthesia 1.5 ml, 2.0 ml, till 2.5 ml in proper order because those rabbits got resistance to the action of an anesthesia. In this case, using anesthesia method examined the neural control characterization of the heart activity with nonlinear dynamics.

Ⅲ. RESULTS

Whole HFECG of 25 healthy dogs physical test indicated that parameters of HFCs range within width of 3.8 mS and amplitude of 84.0 uV after computing them. In this case, we have defined above values as threshold. We called the notching as pathological one if its parameters are over the threshold. Otherwicw, it is called normal which could be distributed all over the range of whole QRS complex. For the convenient of analyzing and studying, the width of range of the dog QRS complex was divided by three segments on time, they are initial segment (<15 ms), middle (15 – 25 ms) and terminal one (>25 ms). The average width for 25 dogs QRS complex was about 40 ms.

As control, wide band ECG contrasted with the 25 normal dogs have some notches and slurs on QRS complex of ECGs. Their numbers and locations were different from each other because of the individual difference. But they could be distinguished one from the others which were with pathological characters. The HFCs especially were observed within several minutes of localized myocardial injection with formalin and persisted during the following experimental period of hours. And the components, clear-cut notches, were also found easily after ligaturing coronary arteries.

Clear-cut notching was measured affirmatively after ligaturing one hour later. Clear-cut slurs also and always appeared within certain minutes (such as 20 minutes) of myocardial injury for either formalin injecting or ligaturing coronary arteries but they were non-idiosyncratic. It signifies the sensitive and dynamical response of HFCs to diagnostic pathological changes of the heart.

As a whole, both ligaturing coronary arteries and injecting formalin to injure myocardial tissues could produce obvious raise and change of HFCs. It has to be noted that we have analyzed the characters of notches and slurs before and after myocardial injury and found that their expression was the most obvious during the following one-hour period of injury. On the basis of long-term chronic observational experiments, the numbers and locations of HFCs were unstable and could change a lot during the following day period (such as within 4-7 days or even more) of observation shown in the statistical Fig.1.

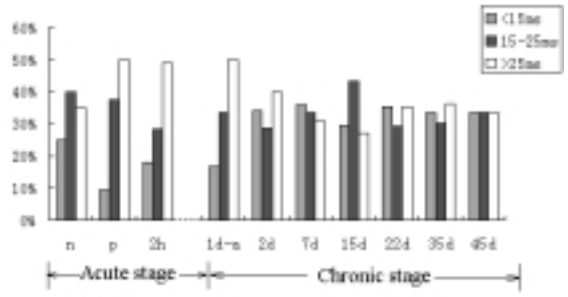

Fig. 1 The variation trend of mean value of total HFC member (notches and slurs) during different experimental periods.

We have repetitively done man-made small wounded cardia1c muscle to simulate heart diseases experiments many times and got good repetitive results.

An anesthesia method was used to study neural control characterization of the heart activity with rabbits.

IV. DISCUSSION

Sensitivity of HFCs (notches and slurs). Owing to HFCs are produced from action potential propagation changes of cardiac cell membrane, so they are very sensitive to response the changes of the heart status and are useful to make use of clinical diagnosis. Such as measuring epicardial potential with bipolar electrode could caused the larger change of HFCs in wide-band ECG on body surface and persisted during the following 2 day period of measurement. After that, the phenomenon automatically disappeared in the dog that meant it suffered “adjacent interference” or even slight wound. This is can be seen that HFECG, especially notches, is very sensitive response heart abnormal environment. Especially, pathological notches were produced by cardiac slight wound.

Idiosyncrasy, fast response and orientation. Our experiments indicate that wide-band ECG of all dogs have notches and slurs which distributed different interval of QRS complex and had different numbers. After thorough computing, their parameters were not the same but within certain scope. This phenomenon was showing no difference to notched ECG apparently healthy subjects including children, youth, adults and old people. In this case, it is no able to explain notches and slurs on normal human and dogs by myocardial-local pathological changes. In this case, we think only counting the total number of slurs and notches as diagnostic indices is insufficient scientific but could be look up total number as a variation track of the heart activity. And we proposed a local parameter, what is called pathological notches used as a diagnostic parameter, and explained, by experimental studies, that the reason for causing HFCs notches and slurs (especially notches) should be divided by normal and pathological notching

In long-term chronic observation, two of dogs had got a piece of injury of cicatricial phase at endocardium for each after cut sections for microscopic examination.

Dynamic features of HFCs. Clear-discernible notches were produced in 14 acute experimental dogs, and they always appeared within one hour of the myocardial injection with formalin and persisted during the following one-hour period of observation. The similar results happened in another 8 chronic experimental dogs, and they measured notches after 10 minutes or 60 minutes of the localized myocardial injury and appeared clear HFC waveform. But the HFCs are not stable and always changed during the following 4-7day even more period of injured by chronic ligature or injected with formalin.

The features of Poincare dispersed-dot plot (PDDP). In this article, we have investigated another parameter, what is called global one, with nonlinear PDDP method to extract the neural control information of the heart activity because the common cardiac abnormalities can often be ascribed to overaction or failure of heart nerves and reflexes. The anesthesia method was used to simulate the overaction or failure of the heart. As a result of analysis methods of linear heart rate variation most using average value, standard deviation, histogram, spectrum analysis and so on, they could analyze the degree of heart rate variation (HRV) in total but concealed the special details of every beat of the heart. The PDDP can reflect variation sensitivity of the heart obviously.

The endogenous regulation and control of the dog hearts was in progress very active during first 4 to 7 days or even more after operation of making pathological model in which HFC can reflect the phenomena but PDDP could show it much better. According to our experiment results, the PDDP method has more sensitivity to global parameter of neural control of the heart such as animal experiments. The experiments of twenty two rabbits and eight dogs have showed that the parameter is sensitive to response about neural control information of the heart shown in fig.2.

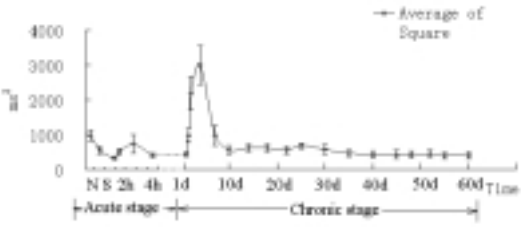

Fig. 2 The average value of PDDP area during the chronic experiments for all dogs.

There is a summit of the curve during 4 to 7 days or even more just explained the dynamical changes of the phenomena in the heart. They illustrated the PDDP can sensitively express the neural control case of the heart suffered block level under different anesthesia condition or diseases.

Both have showed it also sensitively response to dynamic variation of cardiac activity in which a summit of the nonlinear parameter curve has made known the endogenous environment change of the dog heart during the 4 to 7 days or even more after operation.

We have also examined healthy subjects, diabetic patients, single-vessel and multi-vessel disease patients with PDDP method in hospital and found that the long axis has more sensitive then area and short axis parameters. The three parameters have idiosyncrasy about 83%, sensitivity about 70% and coincidental rate about 75%.

Ⅴ. SUMMARY

Our research results suggested that adoptable multi-parameter method to interpret pathological changes of the heart in time could improve clinical diagnostic level of heart diseases. The early pathological changes in the heart can be exposed through early and dynamic analyzing of myocardial-pathological information. The local HFC parameters of the heart can show the pathological changes in heart itself, and global PDDP parameters can demonstrate the neural control troubles of the heart physiological systems. The multi-parameters consisted of local and global indices can make the clinic physicians to understanding patient heart activity more exactly, more systemically and more clearly in order to carry out early diagnosis of heart diseases.

Studying the multi-parameter effects with animal model made small intramural injury were successfully produced in the myocardial wall either formalin injection or ligature of coronary areas 25 dogs. As a diagnostic local pathological changing) parameter, notching needs to go through character extraction and pattern recognition in order to get the pathological notching for early diagnosis in future with doubts.

All dog experiments showed that Q-wave abnormal, R-wave reducing and its duration increasing, ST-segment changing and T-wave standing up side down and so on were caused by heart more serious changes and HFCs (notches and slurs) were caused by a much early and slight changes (especially sluring) so that notching could be used for early diagnosis of heart diseases.

Many common heart diseases such as cardiac failure, arrhythmias and heart block and so on can diagnose by examined neural control of the heart. The PDDP method could act as good actors if HFCs and PDDP are combined in together to diagnose heart diseases in which the diagnostic method could be made progress, diagnosed earlier and faster.

REFERENCE

1. Langner Jr. P. H., (1952), The value of high fidelity electrocardiograph Using the cathode ray oscillograph and an expanded time scale. Circulation, 5, 249-256.
2. Flower N.C., Horan L.G., Thomas J.G., Thomas J.R. and Tolleson W.J. (1996), The anatomic basis for high frequency components in the electrocardiogram. Circulation, 39,31-539.
3. Chien I-C.m., Tompkins W.J. and Briller S.A. (1980), Computer methods for analyzing the high-frequency electrocardiogram. Med Bio. Eng. Comput . 18, 303-312.
4. Ge Jiguang and Tompkins W.J. (1983), High-frequency ECG feature recognition using a high level language. Biom. Scien. Instrum,. 19, 31-34.
5. Ge Jiguang and Tompkins W.J. (1986), High-frequency Electrocardiogram analyzer. IEEE Trans. On Biomedical Engineering. Vol. BME-33, 12, 1137-1140.
6. Ge Jiguang, Xu Yuwei and Dai Jiwang (1994), Pathological change of dog's high frequency ECG under acute myocadial injury, Vol. 28, 692 – 703.
7. Ge Jiguang; Dai Jiwang and Xu Yualei (1997), A pathological model study for high-frequency electrocardiogram with coronary after ligature. Journal of Zhejiang , Vol. 31, 1, 81-92.
8. Goldberger A. L. (1992), Fractal mechanisms, in the electrophysiology of the heart, IEEE Eng. Med. Biol., Vol. 11, 47 – 52.
9. Zhang Hui, Ge Jiguang, Hang Mingjing and Xu Qiuping (1998), Nonlinear dynamics characterization in electrocardiogram, Chinese J. of Biom. Eng. Vol. 17, 214 – 221.